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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUMPHREY, DAVID HAROLD	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,639	HE ET AL.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,32 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicants' election of Group XXII, claims 31-34, without traverse in the reply filed on August 7, 2006.

2. Claims 1-30, 33, and 35, were canceled by Applicants amendment to the claims in the reply filed on August 7, 2006.

Claims 31, 32, and 34, are pending.

Claim 31 is amended.

Claims 31, 32, and 34, are examined on the merits.

Priority

3. Support for the claims 31, 32, and 34, was found in provisional application 60/491,350. Therefore, the priority date for claims 31, 32, and 34, is July 31, 2003.

Sequence Compliance

4. The specification and claims are objected to for failing to adhere to the requirements of the sequence rules. Applicants have not provided the statement that the CRF (computer readable format) submitted and the paper copy of the sequence listings is the same. SEE 37 CFR 1.821 section f). In addition to the paper copy required by paragraph (c) of this section and the computer readable form required by

paragraph (e) of this section, a statement that the content of the paper and computer readable copies are the same must be submitted with the computer readable form, e.g., a statement that "the information recorded in computer readable form is identical to the written sequence listing. "

A reply that fails to comply will be considered to be non-responsive and may result in abandonment of this application.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 9, line 30, and page11, line 1, for example.

Claim Rejections - 35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 31, 32, and 34, are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is vague and indefinite for the recitation of "a Dvl protein". Since there are three known isoforms of Dvl (Dvl-1, Dvl-2, and Dvl-3), it is not clear if the claims are drawn to cancer cells that overexpress one Dvl protein, two Dvl proteins, or all three Dvl proteins. Accordingly, one of ordinary skill would be unable to determine the metes and bounds of the claimed invention.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 31, 32, and 34, are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus. " (See MPEP 2164).

Claim 31 is drawn to a method of inhibiting the growth of a cancer cell that overexpresses a Dvl protein, the method comprising contacting a cell with an *agent* that inhibits Dvl expression. The specification defines an agent that inhibits Dvl expression as a small molecule or an siRNA, see page 4, lines 11-14. Applicants do not provide a sufficient description of a representative number of agents to show that Applicants were in possess of a genus of agents that includes any small molecules and any siRNAs that inhibit any of the Dvl isoforms. There are no identifying characteristics provided in the specification for the sequence of even one species of siRNA used in the invention or for even one species of small molecule that inhibits Dvl expression.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 199 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus.

The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus.

The instant specification does not provide adequate written description to support the claimed genus. The specification does not provide guidance as small molecules or siRNA structures that inhibit the expression of Dvl. Therefore, one of ordinary skill in the art would not recognize from the disclosure that Applicants were in possession of the claimed genus.

To provide adequate written description and evidence of possession of a claimed genus, pro-apoptotic fusion proteins, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, no species of small molecules are provided and the one disclosed species of siRNA is not described. The disclosure of a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the claims encompass numerous species that are not further described. There is substantial variability among the species. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general, guidance is what is needed. Therefore, one of ordinary skill in the art would not recognize from the disclosure that Applicants were in possession of the genus small molecules and siRNAs that inhibit Dvl

expression. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Per the Enzo court's example of a description of an anti-inflammatory steroid couched "in terms of its function of lessening inflammation of tissues," which, the court stated, "fails to distinguish any steroid from others having the same activity or function," and which therefore, fails to satisfy the written-description requirement. Mere idea of function is insufficient for written description; isolation and characterization at a minimum are required.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

10. Claims 31, 32, and 34, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided

by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention and the breadth of the claims: The claims are drawn to a method of inhibiting the growth of a cancer cell that overexpresses a Dvl protein, the method comprising contacting the cell with an agent that inhibits Dvl expression. Claims 32 and 34 provide the limitations that the cancer cell is lung cancer and the agent is siRNA. Therefore, claim 31 encompasses methods of inhibiting the growth of any cancer cell, in vivo as well as in vitro, utilizing any agent that inhibits Dvl expression.

The state of the prior art and the level of predictability in the art: The prior art teaches that members of the Dvl protein family may have different functions and are expressed in different cell types. Okino et al. (Oncology Reports 10: 1219-1223, 2003) teach that Dvl-1 and Dvl-3 share only 64% amino acid homology and their genes lie on different chromosomes, see page 1222, left column, second paragraph, lines 3-6. Okino et al. further teach that although the precise roles of the various molecules in the Dvl family are yet to be elucidated, the function of Dvl-1 is likely divergent from that of Dvl-3 because Dvl-1 appears to participate in the signaling pathway that transduces the Wnt signal to beta-catenin, see page 1222, left column, second paragraph, lines 6-10.

The art teaches that mRNA levels are not always correlated with gene amplification. Okino et al. provide the caveat that while overexpression of mRNA often accompanies gene amplification, other factors, such as transcriptional activation by

hypo-methylation of promoter regions and trans-activation by other cellular molecules, may account for overexpression in some cases, see page 1222, left column, first paragraph, lines 8-12.

In contrast to Applicants invention, overexpression of Dvl proteins has been shown to induce apoptosis in some cell types. Van Gijn et al. (Experimental Cell Research 265: 46-53, 2001) teach that overexpression of Dvl in transformed kidney cells (Cos-1 cells) results in apoptosis, see page 46, right column, first complete paragraph, lines 12-14. Thus the prior art is unpredictable in regards to which cell types overexpress particular isoforms of Dvl protein and what effects overexpression of Dvl protein may have on the cell.

Amount of direction provided by the inventor and the existence of working examples: The specification does not provide support commensurate in scope with the claims. Example 11 discloses a method of inhibiting the growth of one lung cancer cell line, H1703, using siRNA against one Dvl gene, Dvl-3. However, the instant disclosure states in this example that Dvl-1 and Dvl-2 expression were not detected in the tumor samples, see page 48, line 25 through page 49, line 4. Additionally, the specification provides evidence that siRNA does not affect cell growth in another lung cancer cell line A549, or a colon cancer cell line SW480. The specification also does not provide the structure of the siRNA or any small molecules that inhibit Dvl expression. Therefore, one of ordinary skill in the art would conclude that the instant specification is not enabling for a method of inhibiting the growth of any cancer cell or even inhibiting the growth of any lung cancer cell except H1703 with an siRNA for Dvl-3 only. The

specification is also not enabling for a method of inhibiting the expression of Dvl-1 and Dvl-2, since their expression was not detected in the cancer samples.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicants' claim to a method of inhibiting the growth of any cancer cell that overexpresses any Dvl protein. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art such as inhibiting cancer cell growth with any agent that inhibits any Dvl protein expression.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that a method of inhibiting the growth of any cancer cell in vitro or in vivo by contacting the cell with any agent that inhibits expression of any Dvl protein would require undue experimentation in order to use the invention as claimed by the Applicants.

11. Relevant art not relied upon

A. Nagahata et al. Cancer Science 94(6): 515-518, June 2003.

B. Uematsu et al. Oncogene 22: 7218-7221, 2003.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

David Humphrey, Ph.D.

August 20, 2006